

LEADING ARTICLE

Living related liver transplantation: medical and social aspects of a controversial therapy

C E Broelsch, G Testa, A Alexandrou, M Malagó

Gut 2002;50:143–145

There are more than 15 000 patients waiting for a liver transplant in the USA, with an average waiting time of 468 days and a mortality rate as high as 15–20%. Until artificial organs or xenotransplantation becomes a reality, living donor liver transplantation remains the best option for patients with end stage liver disease.

The use of organs, stem cells, or blood products from living donors is widely accepted and contributes towards saving the lives of thousands of patients. Among the solid organs, kidneys, liver, lung lobes, pancreatic segments, and intestines from living donors have all been transplanted with reportedly excellent results. Living donor liver transplantation started in paediatric practice in Chicago¹ in 1989 and is now performed worldwide, particularly in countries where cadaveric organs are not available. It has proved successful in almost eliminating mortality on the paediatric waiting list.² Graft and patient survival are equal and often superior to cadaveric liver transplantation.^{3–4} However, mortality on the waiting list is a growing problem for adult patients affected by end stage liver disease.⁵ Numerous efforts have been made on social and legislative levels to solve this problem. Organ banks, patient organisations, national agencies, and governments have promoted cadaveric donation (United Network Organ Sharing; www.UNOS.org). Liver allocation policies have been changed to favour the sickest patients and transplant them earlier. Marginal organs are now routinely transplanted.⁶ Liver split grafts are more often accepted. Despite all of these efforts there are more than 15 000 patients waiting for a liver transplant in the USA, with an average waiting time of 468 days and a mortality rate while on the waiting list as high as 15–20%, quite apart from the associated morbidity. Thus modern medicine has found the cure to a deadly disease but because of the shortage of organs it cannot provide treatment to thousands of patients.

Living donor liver transplantation among adults offers the only moral and real solution to the problem at the present time.⁷ The operation consists of major hepatic resection where either the right liver lobe including anatomical segments 5–8 or the left liver lobe with segments 2–4 are resected and subsequently transplanted. Interest in the living donor liver transplantation procedure is worldwide.

"Living donor liver transplantation among adults offers the only moral and real solution to the problem at the present time"

In countries where cadaveric donors are not available, living donation constitutes the only possibility of treatment. Hundreds of patients have been transplanted in Japan since the introduction of living donor liver transplantation in the early 1990s.⁸ Interestingly enough, despite new regulations that allow cadaveric organ transplantation, living donor liver grafts remain practically the only significant source of grafts for the Japanese.

In countries where cadaveric organs have historically been the main source of grafts, the implications of a broader acceptance of living donor grafts are several.

(1) Waiting time would be minimal for recipients who have a living donor, and with the redistribution of the cadaveric organs among a smaller number of recipients, other patients who have no possibility for a living donation could be transplanted earlier.

(2) Patients could be transplanted before their clinical condition deteriorates, thereby decreasing postoperative complications, reducing hospital stay, and making the postoperative period smoother. Mortality on the waiting list could decrease dramatically. Most patients who die on the waiting list are chronically ill who develop a complication related to their end stage liver disease (for example, spontaneous bacterial peritonitis or renal failure).⁹ Most of these patients would survive if they were transplanted before the onset of the complication or if a liver was readily available.

(3) Marginal organs could be used only in exceptional situations. We have witnessed the increasing use of grafts from very old donors or donors with a questionable past medical history and unstable clinical conditions at the time of harvest. This practice has undoubtedly increased the number of patients who can be transplanted. On the other hand, patients who receive a marginal organ have, in comparison with those who receive a good organ, decreased survival and decreased graft survival and an increased number of postoperative complications.¹⁰ In contrast, living donor liver grafts are accepted only if proved to be of good quality.¹¹

(4) Together with the extremely short ischaemia time, the chances of prompt functioning of the liver are maximised, and by decreasing the number of postoperative complications, recovery of patients is more rapid. As we have already witnessed after the introduction of living donor liver transplantation in the paediatric population, graft and patient survival will further improve and in general, overall costs for patients affected by end stage disease should decrease.

See end of article for authors' affiliations

Correspondence to:
Professor CE Broelsch,
Department of General
Surgery and
Transplantation, University
Hospital Essen,
Hufelandstr 55, 45122
Essen, Germany;
christoph.broelsch@uni-essen.de

Accepted 17 July 2001

(5) Patients with non-resectable hepatocellular carcinoma, who because of stage T2 or greater presentation are denied access to cadaveric liver transplantation lists,^{12, 13} could find a cure with living related liver transplantation. These patients with multifocal hepatocellular carcinomas, although confined to the liver, or tumours larger than 5 cm in diameter, are probably the most dramatic example of the need for society to redistribute a scarce resource. We have an insufficient number of cadaveric organs and by law the decision is imposed to transplant patients who have the best chance of cure.¹⁴ The choice between a patient affected by primary biliary cirrhosis with a two year survival rate after transplantation of greater than 80% and a patient with a 6 cm large hepatocellular carcinoma who has only a 25% survival rate is plainly evident.¹⁵ However, a 25% survival rate is not much different than that observed in patients with oesophageal or pancreatic cancer¹⁶ in whom we routinely offer surgery and complete therapy. It appears that the only limitation to offering a cure to patients with non-resectable hepatocellular carcinoma is the scarcity of cadaveric organs and not the efficacy of the treatment itself. In living donor liver transplantation, society is no longer responsible for choosing which patient is offered a chance to survive. To offer a chance of cure or significant palliation to these patients does not jeopardise the chances of other patients. Delivery of care is back to normal: doctors offering their patients and families a therapy which may result in a cure.

To sustain these concepts we must act with the highest moral standards and medical knowledge. There must be a high level of trust between the donor, recipient, and doctor. What is technically feasible for a liver resection in a tumour patient may not be for a living donor. What is an acceptable risk in a tumour patient who has no other chance must not be so in a living donor. The trust between the family and doctor lies in the agreement that no such boundaries will be crossed. The benefit for the family as a whole must be clear. We consider the family as an active partner in the transplantation process. They must be fully informed and have total understanding of the risks and benefit. Our job is to control the desire to help the most hopeless cases.¹⁷

"We consider the family as an active partner in the transplantation process. They must be fully informed and have total understanding of the risks and benefit"

On the other hand, the direct relationship between doctors and family can make possible transplants that up to now had been denied on the basis of public/society interests.

The equation is not complete without considering the well being of the donor, both physically and psychologically.¹⁸ The donor must spontaneously offer himself. No other reason apart from his/her desire to help must influence his/her decision. Indirect coercion, in the sense of the pressure felt by anyone to help a sick relative, is a natural reaction to a tragic situation. To consider this pressure as a limiting factor in the spontaneity of the donation is to deny one of the basic rules of social and family interaction. The involvement of professionals outside the transplant teams—for example, social workers or psychologists—has added tremendous value to the psychological evaluation of the donor and helped the donors themselves to better understand the motivations of their gift. It has been our experience that no evaluation process has been completed by a donor who was not fully convinced of his/her decisions and acts. The donor and recipient must be aware of the risks of the procedure. The adult recipient is not a passive figure, in contrast with paediatric living donor transplantation. A child may not have much to say to a parent who offers to donate but an adult may oppose the decision of a family member to donate, moved by the same altruistic love which motivate the potential donor. Minimising the risks of hepatectomy while explaining the procedure to the family, apart

from being immoral, will backfire on all doctors involved in living donor liver transplantation.

Major liver resection in non-cirrhotic patients carries a mortality of 0–5% and a morbidity rate as high as 30%.¹⁹ Data in the past three years in nearly 1000 living liver donors who underwent either a right or left hepatectomy reported a mortality rate of 0.5% and a complication rate of 10–40%.²⁰ Most of the reported complications were mild although some donors have undergone reoperation for bile leak, bleeding, or hernia repair. It is the concept of postoperative complications that needs to be revisited when dealing with living donors. There are no minor or major complications only complications that may alter the recovery of the donor. Reporting of these complications by all surgeons is necessary. A national/international registry, similar to the AST in the USA, reflects the awareness of the medical society of the potential dangers of the procedure and its need to exert some form of peer control on its results.²¹ Report of donor complications to these registries is not mandatory but is, in our opinion, an act of honesty and intelligence. Unfounded rumours or false reporting may lead to external peer control that will discredit the medical profession, limit its actions, and jeopardise the existence of living donor liver transplantation.

At the present time, living donor liver transplantation is the best transplant technique that, together with cadaveric organ transplantation, can reduce mortality, morbidity, and time on the waiting list.^{22, 23} A modern liver transplant centre can achieve this goal by offering its patients all of the liver transplant techniques available, from whole liver cadaveric transplantation, to split cadaveric liver transplantation, or living donor liver transplantation.

"At the present time, living donor liver transplantation is the best transplant technique that, together with cadaveric organ transplantation, can reduce mortality, morbidity, and time on the waiting list"

Living donor transplantation in the Western world must not be seen as an alternative to cadaveric donation. We have to continue to promote cadaveric donation and implement the techniques of liver splitting, thus maximising the utilisation of cadaveric grafts.

The first to benefit are patients who have the option to receive the treatment which best suits their needs according to their clinical condition, time available, type of liver disease, and also their wishes.

The impact of living donor liver transplantation on the public and on the professionals in the field has been tremendous. It has forced many to think about the ethical implications and the limit between what is technically feasible and what is morally acceptable.²⁴ It has opened a debate to revise the indications for liver transplantation for pathologies that up until now were not considered.²⁵

"The impact of living donor liver transplantation on the public and on the professionals in the field has been tremendous"

It has given a new role to the patient and the patient's family in the treatment process.

Until artificial organs or xenotransplantation becomes a reality, thus rendering operating on a healthy subject part of medical history, living donor liver transplantation remains the best option to support cadaveric transplantation in the cure of patients affected by end stage liver disease. Maintaining a straight line between what is technically feasible and what is right for patients and their families is the best method of exploiting the potentials offered by this procedure and of making it acceptable worldwide.

.....

Authors' affiliations

C E Broelsch, G Testa, A Alexandrou, M Malagó, Department of General Surgery and Transplantation, University Hospital Essen, Hufelandstr 55, 45122 Essen, Germany

REFERENCES

- 1 **Broelsch CE**, Whittington PF, Emond JC, *et al*. Liver transplantation in children from living related donors. Surgical techniques and results. *Ann Surg* 1991;**214**:428–37.
- 2 **Otte JB**, de Ville de Goyet J, Reding R, *et al*. Pediatric liver transplantation: from the full-size liver graft to reduced, split, and living related liver transplantation. *Pediatr Surg Int* 1998;**13**:308–18.
- 3 **Goss JA**, Shackleton CR, McDiarmid SV, *et al*. Longterm results of pediatric liver transplantation, an analysis of 569 transplants. *Ann Surg* 1998;**228**:411–20.
- 4 **Emond JC**, Whittington PF, Thistlethwaite JR, *et al*. Transplantation of two patients with one liver. Analysis of a preliminary experience with "split-liver" grafting. *Ann Surg* 1990;**212**:14–22.
- 5 **Everhart JE**, Lombardero M, Detre KM, *et al*. Increased waiting time for liver transplantation results in higher mortality. *Transplantation* 1997;**64**:1300–6.
- 6 **Washburn WK**, Johnson LB, Lewis WD, *et al*. Graft function and outcome of older (≥ 60 years) donor livers. *Transplantation* 1996;**61**:1062–6.
- 7 **Furukawa H**, Kishida A, Omura T, *et al*. Indication and strategy for adult living related liver transplantation. *Transplantation* 1996;**61**:1054–8.
- 8 **Todo S**, Furukawa H, Jin MB, *et al*. Living donor liver transplantation in adults: outcome in Japan. *Liver Transpl* 2000;**6**(Suppl 2):S66–72.
- 9 **Brown RS**, Lombardero M, Lake JR. Outcome of patients with renal insufficiency undergoing liver or liver-kidney transplantation. *Transplantation* 1996;**62**:1788–93.
- 10 **Busutil RW**, Shaked AS, Millis JM, *et al*. One thousand liver transplants the lesson learned. *Ann Surg* 1994;**219**:490–9.
- 11 **Sterneck MR**, Fischer L, Nischwitz U, *et al*. Selection of the living donor. *Transplantation* 1995;**60**:667–71.
- 12 **Klintmalm GB**. Liver transplantation for hepatocellular carcinoma. *Ann Surg* 1998;**228**:479–90.
- 13 **Singer PA**, Siegler M, Whittington PF, *et al*. Ethics of liver transplantation with living donors. *N Engl J Med* 1989;**321**:620–2.
- 14 **Wall WJ**, Marotta PJ. Surgery and transplantation for hepatocellular cancer. *Liver Transpl* 2000;**66**:S16–22.
- 15 **Cohen B**, Amaro JD. Some contemporary ethical considerations related to organ transplantation. *Transplant Int* 1995;**8**:238–43.
- 16 **Sener SF**, Fremgen A, Menck HR, *et al*. Pancreatic cancer: a report of treatment and survival trends for 100,313 patients diagnosed from 1985–1995, using the national cancer database. *J Am Coll Surg* 1999;**189**:1–7.
- 17 **Dossetor JB**. A central paradox in medicine: the ethical tension between self-interest and altruism. In: Land W, Dossetor JB, eds. *Organ replacement therapy: ethics, justice, commerce*. Berlin: Springer, 1991:337–43.
- 18 **Adams RK**. Liver organ donors and informed consent: a difficult minuet. *J Leg Med* 1987;**8**:555–86.
- 19 **Belghiti J**, Hiramatsu K, Benoist S, *et al*. Seven hundred forty seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection. *J Am Coll Surg* 2000;**191**:38–46.
- 20 **Broelsch CE**, Malagó M, Testa G, *et al*. Living donor liver transplantation in adults: outcome in Europe. *Liver Transpl* 2000;**6**(suppl 2):S64–5.
- 21 **Authors for the Live Organ Donor Consensus Group**. Consensus statement on the live organ donor. *JAMA* 2000;**284**:2919–26.
- 22 **Testa G**, Malagó M, Broelsch CE. Living donor liver transplantation in adults. *Langenbecks Arch Surg* 1999;**384**:536–43.
- 23 **Marcos A**, Ham J, Fisher R, *et al*. Single-center analysis of the first forty living donor transplants using the right lobe. *Liver Transpl* 2000;**6**:296–301.
- 24 **Renz JF**, Roberts JP. Long-term complications of living donor liver transplantation. *Liver Transpl* 2000;**6**(suppl 2):S73–6.
- 25 **Emond JC**, Renz JF, Ferrell LD, *et al*. Functional analysis of grafts from living donors. Implications for the treatment of older recipients. *Ann Surg* 1996;**224**:544–52.